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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/774,178	02/01/2001	Tetsuya Ishizuka	P66351US0	7485

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EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	**PAPER NUMBER**
1637	
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04/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/774,178	Applicant(s) ISHIZUKA ET AL.	
	Examiner Cynthia B. Wilder, Ph.D.	Art Unit 1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 22 March 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *22 January 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *11 and 19*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attachment to advisory action..
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Cynthia B. Wilder, Ph.D.
Patent Examiner
Art Unit: 1637

Attachment to advisory Action

1. Applicant's amendment filed on 3/22/2007 is acknowledged and has been entered. Claims 11 and 19 are pending. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below.

Applicant's Traversal

2. Applicant traverses the rejection on the following ground: Applicant states that the Examiner states in the advisory action mailed on 12/20/2006 that there is nothing in Applicant's claims or in the instant specification that teaches or suggest that a minimum concentration of 3.2 to 4.4 mM of ITP is "critical" to the instant invention. Applicant states that the aforesaid telephone conference was initiated in order to elucidate the allegation. Applicant states that the undersigned whether criticality of the ITP concentration of 3.2 mM to 4.4 mM was not evidence by the data represented in application Figures 7 and 8 as explained in the present specification. Applicant states that the Examiner did not find the specification data at issue sufficiently evidence of criticality. Applicant states that more precisely, Applicants understand that the Examiner found the 3.2-4.4 mM ITP concentration to be "optimum" and this, not "critical"". Applicant states that in other words, Applicant s understand that the Examiner maintained the ITP concentration must be "surprising and unexpected" in order to evidence criticality, i.e., patentability over the prior art. Applicant states that the Examiner's findings are not sustainable.

Applicant states that the rejection incorrectly equates and "optimum" difference (over the prior art) with a "non-patentable difference and, moreover, incorrectly requires

a "critical" difference (over the prior art). Necessary for patentability. Applicant states that section 103(a) does not require the invention to an improvement over, or more complex than, the prior art in order to be patentable. Applicant cites several case laws and states that "nothing in the patent statute requires that an invention be superior to the prior art to be patentable. Applicant further states that an invention need not operate differently than the prior art to be patentable, but only be different. Applicant states that since the claims 3.2-4.4 mM ITP concentration is "different" than the prior art the present claims are "patentable over the cited prior art.

Applicant stats that the rejection mistakenly relies on -language taken out of context - *In re Aller*, 105 USPQ 233, 235 (CCPA 1955). Applicant states that the statement of rejection cited Aller in alleging "its not invention discover the optimum or workable ranges by routine experimentation. Applicant states that subsequent case law, e.g., *In re Yates*, 211 USPQ 1149, 1151 (CCPA 1981), has cautioned against reliance on *Aller* by focusing on "routine experimentation" being the (alleged) manner by which the optimum range was discovered. Applicant states that *Yates* clarifies that the issue is whether the claimed range optimum or otherwise, would have been expected in view of the prior art, i.e., not whether the claimed range was discovered as a result of "routine experimentation". Applicant states that since the rejection has failed to show that the skilled artisan would have expected the claimed 3.2-4,4 mM ITP concentration to be the optimum range, the initial burden of establishing a prima facie case of obviousness has not be met. Applicant states that in the context of a rejection for obviousness under 35 USC 103(a), the Examiner bears both the initial burden of

presenting a prima facie case of unpatentability and the ultimate burden of persuasion on the issue. Applicant request the rejection be withdrawn.

Examiner's Response

3. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons that follow: In response to Applicant's arguments concerning the specification's evidence of the claimed concentrations of 3.2-4.4 mM of ITP to be "critical", the Examiner maintains that the specification does not show the concentrations of 3.2-4.4 mM of ITP to be "critical". A review of the specification and Figures 7 and 8 show the concentration of between 3.2 and 4.4 mM to give the shortest rising time as compared to control. These concentrations however did not give the highest relative fluorescence intensity (see figures 2, 3, 4, 7 and 8). In fact, based on Applicant's data, the highest fluorescent intensity was seen as a concentration of 1.0 mM (see Figure 2). As stated in the prior Office action, Applicant merely performed a dose curve analysis through routine experimentation wherein ITP concentrations from 0 to 4.4 mM were analyzed in an amplification reaction (see specification at Figures 2, 3, 4, 7 and 8). Specifically, the specification teaches that the concentrations of ITP included 0, 0.1, 0.5, 1, 1.5, 2.0, 2.5, 2.7, 2.8. 3.0, 3.2, 3.6, 4.0, 4.4 mM (see Figures). The results showed that a concentration of between 3.2 to 4.4 MM of ITP was the fastest.

The cited prior art, Nakahara provides a similar teaching in that the reference discloses a dose curve analysis wherein ITP concentrations from 0-4 mM are utilized in an amplification reaction. Specifically, Nakahara discloses wherein the ITP

concentrations include 0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5 and 4.0 mM. Like Applicant, Nakahara discloses wherein a concentration of 3.0 to 4.0 effectively provided an increase in fluorescent intensity of an amplification product over that of the control (see Figure 1, page 1855). MPEP 2144.05 states that "[I]n the case where the claimed ranges **"overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists.** *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)." MPEP further states that **"[S]imilarly, a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties.** *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)." In this case, it is clear that the concentrations of ITP recited in the prior art overlap and are close enough that one skilled in the art would have expected them to have the same properties as those recited in the instant invention. Thus, this argument is not found persuasive.

In regards to Applicant's arguments that the 3.2-4.4 mM ITP concentration is "different" than that of the prior art, the Examiner disagrees for the reasons stated above. To reiterate, the prior art teaches a concentration of 0-4mM of ITP which overlaps with the concentrations of 3.2-4.4 mM of ITP as recited in the instant invention. This argument is not found persuasive.

In regards to Applicant's arguments that the Examiner has taken *In re Aller* out of context, the Examiner respectfully disagrees. Again it is noted that the instant

specification has not provided any evidence to support that the claimed concentration of 3.2-4.4 mM of ITP is "critical" to the instant invention. Rather, the specification has shown that an *"optimum"* concentration for getting the shortest rising time over control is at those concentrations. These concentrations did not give the greatest ratio of fluorescent intensity nor was there any evidence, which suggest that the lower concentrations of ITP would not result in an increase in the amplification products. There is nothing in Applicant's disclosure which resulted in a difference over the prior art as the prior art "expected" ITP to *increase* the yield of the amplification product as evidence by the title of Nakahara's prior art document and the Figure 1 at page 1855.

MPEP 2144.05 states that "[G]enerally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The Examiner maintains that Applicant's invention attempts to determine optimum concentrations of ITP through routine experimentation (dose curve analysis) to determine which concentrations gives the greatest ratio of fluorescence intensity and which concentrations gives the fastest results (see Figures). It is again noted that "it is not inventive to discover the optimum or workable ranges by routine experimentation." Applicant's arguments are not sufficient to overcome the prior art rejections under 35 USC 103(a). Accordingly, the rejections are maintained.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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